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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/483,434	01/14/2000	JEFFERY L. MILLER	14014.0360	8390

23859 7590 09/23/2002  
NEEDLE & ROSENBERG P C  
127 PEACHTREE STREET N E  
ATLANTA, GA 30303-1811

EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 09/23/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/483,434

Applicant(s)

MILLER ET AL.

Examiner

Gerald G Leffers Jr.

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 June 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 02 July 2002. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: the limitation of "streptavidin" in the new and amended claims raises new issues of art.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 9 and 10.

Claim(s) objected to: 3, 7, 17 and 18.

Claim(s) rejected: 1, 2, 15 and 16.

Claim(s) withdrawn from consideration: 4, 5, 8 and 11-14.

8. ☐ The proposed drawing correction filed on \_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_.
10. ☐ Other: \_\_\_\_

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***Advisory Action Attachment***

Continuation of 5. does NOT place the application in condition for allowance because: applicants' arguments are not persuasive on several grounds. With regard to rejection of claims 1-2 and 15-16 for lack of description under 35 USC 112 1st paragraph, applicants' response essentially argues: 1) the examiner improperly did not consider those elements of enablement that are relevant to written description, 2) applicants suggest that the examiner did not consider the application and cited references with regard to the state of the art at the time of filing as someone of skill in the relevant art would consider them, 3) the examiner improperly sets a standard that the cited references must teach each and every element of the claimed invention, 4) the invention is novel in the art, making it impossible for any single reference to provide each and every aspect of the inventions, 5) the references demonstrate the high state of the art regarding processes and steps that can be taken to provide the present invention and that one of skill in the art, recognizing clearly the many different ways of accomplishing and using the invention using the common knowledge of the art, 6) one of skill in the art would recognize that artificial ligands could be used in the invention, 7) those of skill in the art would readily recognize those chemistries used for cross-linking molecules are known in the art , 8) there are methods of covalently linking molecules that are based upon the same chemistry as used for cross-linking avidin or biotin to molecules, 9) one of skill in the art would clearly recognize that virtually any molecule containing and/or capable of being modified to contain a primary amine could be attached to the surface of a cell using reagents routinely used in the examples of the present application, 10), it is not necessary that one of skill in the art knows that a particular type of cross-linking chemistry result in viable cells bearing the covalently linked receptor for one to

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recognize that applicants were in possession of the claimed invention, 11) applicants submit that the many examples of the invention that would necessarily be recognized by those of skill in the art to fall within the scope of what the inventors considered their invention is an adequate number of species to support the broader genus describe in claims 1 and 15 .

With regard to the assertion that the examiner did not properly consider those elements required for a proper enablement rejection that are also necessarily important to rejections for lack of written description (e.g. the state of the art, predictability of the art), this assertion is inaccurate. While the examiner did state that assertions directed towards enablement of the claimed invention were not relevant to the instant rejection for lack of written description, this statement was clearly made in response to the mischaracterization of the original rejection as being made on the grounds of enablement (e.g. "In light of the substantial evidence of the skill of the art at the time this application was filed, Applicants respectfully assert that the Examiner's assertion of lack of enablement is rebutted." (Paper No. 13, page 10, last paragraph). Nowhere did the examiner indicate that the state of the art, predictability of the art, etc., were not considered in making the original rejection, or in maintaining the rejection. In fact, all of the relevant factors have been considered with regard to the original specification and the cited references in making and maintaining the instant rejection.

The examiner has not in any way indicated that all of the elements of the claimed invention must be taught in a single reference, or even in a number of references. However, teachings in the art that demonstrate the covalent linkage of molecules to the surface of a cell would necessarily make it more predictable for one of skill in the art to envision specific embodiments of the broadly claimed genus of receptor/ligand/cell combinations. The attachment

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of the molecule to the cell surface is a critical element of the invention. Viability of the cell following the attachment of the molecule/receptor to the cell surface also appears to be a critical element of the claimed invention because there is no description anywhere in the specification where a molecule/receptor is attached to the surface of a dead cell. No utility has been described in the specification for embodiments of the claimed methods where the cell has not survived attachment of the molecule/receptor (after all, the claims state that the molecule/“receptor” must be capable of binding a ligand complex and incorporating the ligand complex into the cell). Thus, the chemical method of attachment of the molecule/receptor to the surface of the cell is relevant and it is important for one of skill in the art to be able to envision those methods that would allow a cell to survive attachment. The cited references that are directed towards conjugation methods that are done in free solution don't adequately address this issue. They provide no basis for one of skill in the art to extrapolate the structural/functional characteristics of methods of conjugation of molecules in free solution to conjugation of molecules on the surface of a cell such that the cell survives and is capable of incorporating a ligand bound to the molecule/“receptor” into the cell.

With regard to the general assertions made in applicants response that the cited references demonstrate the high state of the art regarding processes and steps that can be taken to provide the present invention, or that the many examples of the invention recognizable to one of skill in the art would describe the broadly claimed, the assertions are not supported in applicants' response, the instant specification or in the teachings of the cited references. Again, the general teachings of the cited references do not provide a means for one of skill in the art to envision a sufficient number of specific embodiments of the claimed invention (i.e. cell surface-

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“receptor”/ligand-biologically active molecules) to describe the broadly claimed genus. For example, even if one concedes that other embodiments of the claimed invention may be envisioned based upon a common chemistry for attachment with that used for biotin/avidin (which is not conceded here), the claims encompass literally any combination of molecule/ligand wherein the molecule/“receptor” is attached to the cell surface by any means (i.e. by any type of chemistry to any reactive group on any structural element of the cell surface). Therefore, a description of one type of chemistry used to attach a molecule (e.g. by primary amines on the cell surface using the same class of cross-linkers used to attach biotin to the cell surface) cannot be considered as descriptive of the broadly claimed genus. How are the reactive groups attached to what portions of what cell surface molecules such that the molecule/“receptor” functions to transport a bound ligand complex into the cell? As indicated in the previous office action, the applicants have not provided sufficient teachings from the prior art to offset the deficiencies of the instant specification with regard to providing a structural/functional basis for one of skill in the art to envision a sufficient number of different species to describe the broadly claimed genus of combinations of cell surface-“receptor”/ligand-biologically active molecules.

It is noted that applicants appear to be relying upon the teachings of the cited references to provide enabling and descriptive support for embodiments of the claimed invention that are not described in the instant specification. To the extent that these teachings are essential to the claimed invention, the incorporation of these teachings by reference is improper.

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***Conclusion***

The proposed amendment has not been entered. Claims 9-10 are allowed. Claims 3, 7 and 17-18 are objected to as being dependent upon a rejected claim. Claims 1-2 and 15-16 are rejected. Claims 4-5, 8 and 11-14 are withdrawn from consideration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.  
Examiner  
Art Unit 1636

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ggl  
September 17, 2002

DAVID GUZO  
PRIMARY EXAMINER  
*David Guzo*